Amendments to the Claims

Please amend Claims 86 and 92. The Claim Listing below will replace all prior versions of the claims in the application:

Claim Listing

- 1. (Previously presented) A method of treating an inflamed orthopedic joint, said joint comprising i) opposing hyaline cartilage articular surfaces, ii) a peripheral collagenous capsule defining a central joint space and iii) synovial fluid contained within the joint space, comprising trans-capsularly administering into the joint space a formulation comprising an effective amount of an inhibitor of TNF-α synthesis, wherein the inhibitor of TNF-α synthesis is an anti-TNF-α monoclonal antibody or antigen-binding fragment thereof such that the inflamed orthopedic joint is treated.
- 2. (Original) The method of claim 1, wherein the joint is a knee joint.
- 3. (Withdrawn) The method of claim 1, wherein the joint is a hip joint.
- 4. (Withdrawn) The method of claim 1, wherein the joint is a spinal facet joint.
- 5. (Withdrawn) The method of claim 1, wherein the high specificity antagonist is an inhibitor of a pro-inflammatory interleukin.
- 6. (Withdrawn) The method of claim 5, wherein the interleukin is IL-1 β .
- 7. (Withdrawn) The method of claim 5, wherein the interleukin is IL-2.
- 8. (Withdrawn) The method of claim 5, wherein the interleukin is IL-6.
- 9. (Withdrawn) The method of claim 5, wherein the interleukin is IL-8.
- 10. (Withdrawn) The method of claim 5, wherein the interleukin is IL-12.
- 11. (Withdrawn) The method of claim 5, wherein the interleukin is IL-19.

- 12. (Withdrawn) The method of claim 1, wherein the high specificity antagonist is an inhibitor of membrane-bound TNF- α .
- 13. (Withdrawn) The method of claim 12, wherein the high specificity antagonist is also an inhibitor of soluble TNF- α .
- 14. (Canceled).
- 15. (Withdrawn) The method of claim 1, wherein the high specificity antagonist is an inhibitor of a natural receptor of TNF-α.
- 16. (Withdrawn) The method of claim 1, wherein the high specificity antagonist is an inhibitor of p38 kinase selected from the group consisting of:
 - a) diaryl imidizole;
 - b) N,N'-diaryl urea;
 - c) N,N-diaryl urea;
 - d) benzophenone;
 - e) pyrazole ketone;
 - f) indole amide;
 - g) diamides;
 - h) quinazoline;
 - i) pyrimido [4,5-d]pyrimidinone; and
 - j) pyridylamino-quinazoline.
- 17. (Withdrawn) The method of claim 1, wherein the high specificity antagonist is an inhibitor of p38 kinase that is substantially water insoluble.
- 18. (Withdrawn) The method of claim 1, wherein the high specificity antagonist is a 1-aryl-2-pyridinyl heterocycle is selected from the group consisting of:
 - a) 4,5 substituted imidazole;
 - b) 1,4,5 substitutued imidizole;
 - c) 2,4,5 substututued imidizole;
 - d) 1,2,4,5 substituted imidizole; and

- e) non-imidizole 5-membered ring heterocycle.
- 19. (Withdrawn) The method of claim 1, wherein the high specificity antagonist is an inhibitor of NO synthase.
- 20. (Withdrawn) The method of claim 19, wherein the high specificity antagonist is L-NIL.
- 21. (Withdrawn) The method of claim 19, wherein the high specificity antagonist is N^G monomethyl-L-arginine.
- 22. (Withdrawn) The method of claim 1, wherein the high specificity antagonist is an inhibitor of PLA₂.
- 23. (Withdrawn) The method of claim 1, wherein the antagonist is an anti-proliferative agent.
- 24. (Withdrawn) The method of claim 23, wherein the anti-proliferative agent comprises rapamycin.
- 25. (Withdrawn) The method of claim 23, wherein the anti-proliferative agent comprises a cdk inhibitor.
- 26. (Withdrawn) The method of claim 23, wherein the anti-proliferative agent comprises a statin.
- 27. (Withdrawn) The method of claim 23, wherein the anti-proliferative agent comprises an anti-oxidant.
- 28. (Withdrawn) The method of claim 27, wherein the anti-oxidant comprises a super oxide dismutase.
- 29. (Withdrawn) The method of claim 1, wherein the high specificity antagonist comprises an inhibitor of an MMP.
- 30. (Withdrawn) The method of claim 1, wherein the joint is a sacro-iliac joint.

- 31. (Withdrawn) The method of claim 1, wherein the high specificity antagonist is an apoptosis inhibitor and is selected from the group consisting of EPO mimetic peptide and an EPO mimetibody.
- 32. (Withdrawn) The method of claim 1, wherein the high specificity antagonist is an apoptosis inhibitor and is selected from the group consisting of IGF-I and IGF-II.
- 33. (Withdrawn) The method of claim 1, wherein the high specificity antagonist is a caspase inhibitor.
- 34. (Previously Presented) The method of claim 1, wherein the formulation further comprises at least one growth factor.
- 35. (Withdrawn) The method of claim 34, wherein the additional therapeutic agent comprises glycosaminoglycans.
- 36. (Original) The method of claim 1, wherein the formulation further comprises a liposomal delivery system.
- 37. (Original) The method of claim 1, wherein the formulation is administered in an amount of less than 1 cc.
- 38. (Previously Presented) The method of claim 1, wherein the inhibitor of TNF- α synthesis is present in the formulation in an amount of at least 100 mg/ml.
- 39. (Original) The method of claim 1, wherein the formulation further comprises a sustained release device.
- 40. (Original) The method of claim 39, wherein the sustained release device comprises a hydrogel.
- 41. (Original) The method of claim 39, wherein the sustained release device provides controlled release.
- 42. (Original) The method of claim 39, wherein the sustained release device provides continuous release.

- 43. (Original) The method of claim 39, wherein the sustained release device provides intermittent release.
- 44. (Canceled).
- 45. (Original) The method of claim 39, wherein the sustained release device comprises microspheres having a plurality of degradation rates.
- 46. (Previously presented) The method of claim 39, wherein the sustained release device maintains the administered inhibitor of TNF-α synthesis at a therapeutically effective level.
- 47. (Original) The method of claim 1, wherein the formulation is provided closely adjacent to the outer wall of the capsule.
- 48. (Previously Presented) The method of claim 1, wherein the inhibitor of TNF- α synthesis is present in the formulation in a maximum amount of 0.5 mg.
- 49. (Canceled).
- 50. (Previously presented) The method of claim 1, wherein the formulation further comprises a growth factor is provided by platelet concentrate.
- 51. (Previously Presented) The method of claim 1, wherein the inhibitor of TNF-α synthesis therapeutically inhibits the production of a cytokine.
- 52. (Withdrawn) The method of claim 1, wherein the formulation further comprises viable mesenchymal stem cells.
- 53. (Original) The method of claim 1, wherein the formulation is injected into the synovial fluid.
- 54. (Original) The method of claim 1, wherein the formulation includes a viscosupplement.
- 55. (Previously Presented) The method of claim 1, wherein a portion of the synovial fluid is removed prior to administration of the inhibitor of TNF-α synthesis.

- 56. (Original) The method of claim 1, wherein the administration is performed through a needle.
- 57. (Original) The method of claim 1, wherein the formulation is administered through a drug pump.
- 58. (Original) The method of claim 1, wherein the formulation is administered in a volume of between 0.03 ml and 0.3 ml.
- 59. (Canceled).
- 60. (Original) The method of claim 1, wherein the administration comprises providing the formulation in a patch attached to an outer wall of the capsule.
- 61. (Original) The method of claim 1, wherein the administration comprises providing the formulation in a depot at a location closely adjacent an outer wall of the capsule.
- 62. (Original) The method of claim 1, wherein the administration comprises providing the formulation in a depot at a location closely adjacent to an endplate of an adjacent bony body.
- 63. (Previously Presented) The method of claim 1, wherein the inhibitor of TNF-α synthesis is predominantly released from the formulation by diffusion of the high specificity antagonist through a sustained delivery device.
- 64. (Original) The method of claim 63, wherein the sustained delivery device is a polymer.
- 65. (Previously Presented) The method of claim 1, wherein the inhibitor of TNF-α synthesis is predominantly released from the formulation by biodegradation of a sustained delivery device.
- 66. (Withdrawn) A method of therapeutically treating a degenerating joint, comprising:
 - a) determining a level of a pro-inflammatory protein within the joint,
 - b) comparing the level against a pre-determined level of the proinflammatory protein, and

- c) injecting an antagonist of the pro-inflammatory protein into the joint.
- 67. (Withdrawn) The method of claim 66, wherein the proinflammatory protein is an interleukin.
- 68. (Withdrawn) The method of claim 67, wherein the predetermined level for the interleukin is at least 100 pg/ml.
- 69. (Withdrawn) The method of claim 66, wherein the proinflammatory protein is an interleukin-6.
- 70. (Withdrawn) The method of claim 69, wherein the predetermined level for the interleukin-6 is at least 100 pg/ml.
- 71. (Withdrawn) The method of claim 69, wherein the predetermined level for the interleukin-6 is at least 250 pg/ml.
- 72. (Withdrawn) The method of claim 66, wherein the proinflammatory protein is an interleukin-8.
- 73. (Withdrawn) The method of claim 72, wherein the predetermined level for the interleukin-8 is at least 500 pg/ml.
- 74. (Withdrawn) The method of claim 66, wherein the proinflammatory protein is PGE2.
- 75. (Withdrawn) The method of claim 74, wherein the predetermined level for PGE2 is at least 1000 pg/ml.
- 76. (Withdrawn) The method of claim 66, wherein the proinflammatory protein is TNF-α.
 - 77. (Withdrawn) The method of claim 76, wherein the predetermined level for TNF- α is at least 20 pg/ml.
 - 78. (Withdrawn) The method of claim 76, wherein the predetermined level for TNF- α is at least 30 pg/ml.

- 79. (Withdrawn) The method of claim 66, wherein the predetermined level for TNF-α is at least 1000 pg/joint.
- 80.-83. (Canceled).
- 84. (Withdrawn) A method of treating an inflamed orthopedic joint, wherein inflammation of the orthopedic joint results in ankylosing spondylitis, said joint comprising i) opposing hyaline cartilage articular surfaces, ii) a peripheral collagenous capsule defining a central joint space and iii) synovial fluid contained within the joint space, comprising transcapsularly administering into the joint space a formulation comprising an effective amount of an inhibitor of TNF-α synthesis such that an inflamed joint is treated.
- 85. (Withdrawn) The method of Claim 84, wherein said inhibitor of TNF-α synthesis is infliximab.
- 86. (Withdrawn-currently amended) The method of Claim 84, wherein said inhibitor of TNF- α synthesis is adalimulab adalimumab.
- 87. (Withdrawn) The method of Claim 84, wherein said inhibitor of TNF- α synthesis is CDP-571.
- 88. (Withdrawn) The method of Claim 84, wherein said inhibitor of TNF- α synthesis is CDP-870.
- 89. (Canceled).
- 90. (Canceled).
- 91. (Previously presented) The method of claim 1, wherein the formulation further comprises BMP-1, BMP-3, BMP-2, OP-1, BMP-2A, BMP-2B, or BMP-7.
- 92. (Currently amended) The method of Claim 1, wherein the formulation further comprises TGF-B TGF-β.

10/630,227 -10-

- 93. (Previously presented) The method of Claim 1, wherein said inhibitor of TNF- α synthesis is adalimumab.
- 94. (Previously presented) The method of Claim 1, wherein said inhibitor of TNF- α synthesis is CDP-571.
- 95. (Previously presented) The method of Claim 1, wherein said inhibitor of TNF- α synthesis is CDP-870.
- 96. (Previously presented) A method of treating an inflamed orthopedic joint, said joint comprising i) opposing hyaline cartilage articular surfaces, ii) a peripheral collagenous capsule defining a central joint space and iii) synovial fluid contained within the joint space, comprising trans-capsularly administering into the joint space a formulation comprising an effective amount of an inhibitor of TNF-α synthesis, wherein the inhibitor of TNF-α synthesis is infliximab, such that the inflamed orthopedic joint is treated.